

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:

**Trautman, et al.**

**FOR: APPARATUS AND METHOD  
FOR PIERCING SKIN WITH  
MICROPROTRUSIONS**

**SERIAL NO: 09/976,798**

**FILED: October 12, 2001**

**ART UNIT NO: 3763**

**EXAMINER: Thompson, Kathryn L.**

**DOCKET NO: ARC 3043 R1**

**DECLARATION -- UNDER RULE 1.132**

I, Robert T. Stone, declare as follows:

1. I received a Bachelor of Science Degree in Electrical Engineering (BSEE) from Virginia Polytechnic Institute and State University in 1977; a Master of Science Degree in Electrical Engineering (MSE) from Virginia Polytechnic Institute and State University in 1979; and a Doctorate Degree (PhD) in Electrical Engineering from Stanford University in 1981.

2. I have over thirty (30) years of academic and industry experience in the field of medical systems and instrumentation, including devices and methods for delivering agents to a subject.

3. I was formerly Vice President of Research and Development, Chief Technical Officer, of Natus Medical, Inc. and am currently Chief Operating Officer, Chief Technical Officer of MedTech Development, LLC, a research and development group with primary emphasis on the medical devices and systems.

4. I am also a named inventor in over twenty (20) issued U.S. Patents and several pending U.S. Patent Applications in the medical field.

5. I am very familiar with the above-referenced patent application, PCT Application Nos. US97/23274 (WO 98/28037) to Theeuwes, et al. and EP95/04660 (WO 96/17648) to Effenhauser, et al., and U.S. Pat Nos. 3,964,482 to Gerstel, et al., 5,279,544 to Gross, et al. and 5,879,326 to Godshall, et al. I am also familiar with significant prior art relating to passive and active (e.g., iontophoresis) transdermal delivery apparatus and systems.

6. As discussed in greater detail herein, the specification of the subject application provides a *clear* teaching that applying a microprotrusion member to the stratum corneum with the claimed impact energy parameters provides several significant, stated advantages, achieves at least one particular purpose and solves at least one stated problem. Further, the impact energy disclosed and claimed in the subject application is neither disclosed, taught or suggested by any of the noted prior art reference, nor is it an obvious matter of design choice to impact the stratum corneum with a power of at least 0.05 joules/cm<sup>2</sup> of the microprotrusion member in 10 milliseconds or less, as claimed in the subject application.

7. In my opinion, the specification clearly discloses several major benefits and, hence, advantages associated with applying a microprotrusion member by impacting the stratum corneum with the claimed energy. One major benefit disclosed in the subject application is the creation of uniform, effective penetration of the stratum corneum without undue patient discomfort, which is not taught or suggest by any known prior art reference. This teaching is reinforced by Examples 1 and 2, which clearly demonstrate that the application of the microprotrusion member with the claimed power parameters results in effective penetration of the stratum corneum and, hence, an increased rate of agent delivery.

8. Prior art means of applying a microprotrusion member typically result in significant variations in puncture depth across the microprotrusion array and in large variations in puncture depth between applications. The specification on page 8 of the subject application clearly discloses that the invention solves these problems by applying the microprotrusion member to the stratum corneum with the claimed impact energy, whereby the microprojections effectively and consistently pierce the stratum corneum.

9. Theeuwes, et al. neither provides teaching that would allow one to apply a microprotrusion member to the stratum corneum with the claimed energy in the specified time, nor motivate one to do so to realize the advantages clearly disclosed in the subject application. Indeed, none of the noted references, alone or in combination, even recognize the problems solved by the claimed application parameters or even suggest an energy of application.

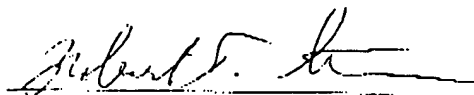
10. A further benefit associated with the application of a microprotrusion member to the stratum corneum with the claimed impact energy accrues as a result of the hold-down spring force which optimally tensions the skin for the impact driven penetration. It is the combination of the impact energy delivery, resultant impact velocity, residual force in the piston spring, tension of the skin (as maintained by the hold-down spring force required for actuation of the piston), which results in the optimum performance parameters described and claimed. This combination of parameters as an optimum is not obvious to one skilled in the art and would require extensive experimentation to determine.

11. The experimental results set forth in the subject application also reflect a further benefit associated with the application of a microprotrusion member to the stratum corneum with the claims impact energy -- enhanced transdermal delivery of the active agent as compared to manual application of a microprotrusion member, which is inherently taught by Theeuwes, et al.

12. A further benefit associated with the application of a microprotrusion member to the stratum corneum with the claims impact energy is also reflected in Examples 1 and 2 of the subject application, which clearly demonstrate that uniform and "consistent" penetration can be achieved by use of the claimed impact energy, which facilitates improved transdermal delivery as compared to the manual application of the prior art.

12. One would not expect equal performance with the application parameters and/or methodology (i.e., measurement) taught by the noted references and the claimed application parameters set forth in the subject application. Indeed, as set forth in the subject application, a microprotrusion member applied with the claimed impact energy clearly provides improved delivery over a manually applied microprotrusion member, which is inherently taught by the cited references. The claimed invention thus represents a significant advantage over the delivery methods taught by the noted prior art.

Executed this 4th day of April, 2005 in Los Altos, CA



Dr. Robert T. Stone